REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-13 were pending in this application when last examined.

Claims 1-8, 10 and 11 were examined on the merits and stand rejected.

Claims 9, 12 and 13 are withdrawn as non-elected subject matter.

Claims 1-3 are amended to clarify the claimed invention. Applicants note that all of the examples given in the specification use a ligand-binding domain (LBD) as the ligand recognition site.

No new matter has been added.

On pages 3-6 of the Office Action, claims 1-8, 10 and 11 were rejected under 35 U.S.C §103(a) as obvious over Weatherman et al., Sato et al. and Honda et al. Applicants respectfully traverse this rejection. Initially, it is noted that the claims have been limited to a minimum requirement of a ligand binding domain (LBD) instead of a ligand-recognition site containing such domain.

The requirements for LBD in this invention are:

i) binding of a specific ligand; and

ii) upon binding the ligand, forming a coactive-binding cite to which a peptide (ex. LXXLL peptide) binds.

Weatherman et al. uses full length estrogen receptor (ER), which consists of the AF1 domain, a DNA-binding domain and a ligand-binding domain. In other words, Weatherman et al. fails to teach or suggest if a coactive-binding site is formed by an LBD alone.

The claimed invention was made from a finding that the LBD of nuclear receptors has the requirements i) and ii) shown above. This finding makes it possible to form a "one-molecule type probe" for detecting an agonist or an antagonist to a nuclear receptor. It may be impossible for the full-length receptor to make a one-molecule type probe since it has a large molecular weight. In fact, Weatherman et al. describe a "two-molecule type probe" (ER-RFP and CFP-LXXLL).

A one-molecule type probe is advantageous for measuring FRET phenomenon. In the measurement of FRET in a two-molecule type probe, it is required to equalize the amounts of one probe (ER-RFP) and other probe (CFP-LXXLL) in a cell, because the measuring index of FRET is the fluorescent intensity ratio of the two fluorescent proteins. However, equalization of the levels of two probes is very difficult. On the other hand, there is no problem with equalization of the one-molecule type probe of this invention.

LBD has another advantage over a full-length nuclear receptor. The full-length receptor has various domains corresponding to various functions of the nuclear receptor, which includes DNA-binding. Therefore, one probe (ER-RFP) of Weatherman et al. localizes on chromosomal DNA in a cell (please see Fig. 2 of Weatherman et al.). This restricts applications of the probe. On the other hand, the probe of this invention can function at any portion in a cell, since it does not have unnecessary domains.

Neither Sato et al. or Honda et al. remedy this deficiency of Weatherman et al. In particular, in view of these references, a person of skill in the art would not understand that a probe with merely the ligand-binding domain of the nuclear receptor would properly function. Thus, a person of skill in the art would not have a reasonable expectation of success in substituting the phosphorylation-recognition domain of Sato et al. with an LBD to arrive at the claimed invention.

Thus, for the above-noted reasons, this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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